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ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/916,443	EATON ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 14 February 2007 in which claim 28 was amended, no claims were canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 28-39 are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. It is noted that a prior art reference is considered as a whole and for all it stands for. Thus, while the rejections listed below present a modified interpretation of the teachings of Hilvert et al and Ellington et al solely for the purpose of clarity, the rejections of the claims are maintained for the reasons of record. While Applicant has amended the claims, the amendments do not affect the claimed invention. Thus, the claims are still anticipated by Hilvert et al and Ellington et al as discussed below.

It is further noted that while Mullis et al, Paul, and Rodwell et al are a new pieces of art that have been placed on the record, they is provided only as evidence that that catalysts facilitate chemical reactions. Thus, the claims remain rejected under the same prior art.

5. Claims 28 and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993) in view of Ellington et al (Nature, 1992: 355, pp. 850-852), as evidenced by Mullis et al (U.S. Patent No. 4,965,188, issued 23 October 1990), Paul (U.S. Patent No. 5,236,836, issued 17 August 1993), and Rodwell et al (U.S. Patent No. 5,196,510, issued 23 March 1993).

Regarding claim 28, Hilvert et al teach a method for producing a cyclohexene derivative product library. In a single exemplary embodiment, Hilvert et al teach contacting a mixture of first reactants with a mixture of free reactants, wherein the reactants are dienes and dieneophiles; namely, a plurality of reaction products, which is a product library, are produced by a mixture of diene reactants and dienophile reactants in a Diels Alder reaction (column 24, lines 55-65), and wherein the reactants are racemic (column 26, lines 20-35), and are thus mixtures of reactants that produce a library of cyclohexene derivative products.

While Hilvert et al teach the reaction is facilitated by a catalytic antibody (Abstract), and that it is beneficial to find a specific catalyst for a Diels-Alder reaction (column 5, lines 15-17), Hilvert et al do not specifically teach nucleic acid catalysts for facilitating the reaction.

However, Ellington et al teach that nucleic acid aptamers are be new catalysts for chemical transformations that are analogous to catalytic antibodies (page 852, column 2, last paragraph). Ellington et al further teach the nucleic acid aptamers have the added advantage of allowing large numbers (i.e., 2-

$3x10^{13}$) of potential catalysts to be produced using common synthetic methodology (i.e., using PCR; page 850, column 1-last paragraph). This increases the probability of finding a superior catalyst.

Mullis et al teach defines catalysis as facilitating (column 7, lines 41-45). Paul also equates "catalyze" with "facilitate" (column 1, lines 40-45). Rodwell further defines catalysts as "facilitating" chemical reactions (column 16, lines 10-12). Thus, the catalysts for chemical transformation taught by Ellington et al (page 852, column 2, last paragraph) and the Diels-Alder catalyst as taught by Hilvert et al (column 5, lines 15-17) both encompass the broadly claimed reaction "facilitated by the nucleic acid coupled to said reactant" at the end of claim 1.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to modify the method of preparing a cyclohexene derivative product library of Hilvert et al with the nucleic acid catalyst of Hilvert to couple with a first reactant (e.g., the *first* reactant dienophile or diene of instant claim 28) and catalyze the Diels-Alder reaction with a free reactant (e.g., the *free* reactant diene or dienophile) with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method having the added benefit of increasing the probability of finding a superior catalyst by allowing large numbers of potential catalysts to be produced using common synthetic methodology as explicitly taught by Ellington et al page 850, column 1-last paragraph).

Regarding claim 32, the method of claim 28 is discussed above. Ellington et al also teach the use of DNA oligomers having a region of conserved sequences; namely, defined primer-binding sites (page 850, column 1, paragraph 2, lines 2-3) and a region of randomized sequences (page 850, column 1, paragraph 2, lines 1-2).

Regarding claim 33, the method of claim 28 is discussed above. Ellington et al teach the use of single-stranded DNA (page 850, column 1, paragraph 2, lines 4-6), and that the methods are similar to those used for RNA (Abstract, lines 1-4).

Regarding claims 34 and 35, the method of claim 28 is discussed above. Ellington also teaches that different single-stranded DNA oligomers can be selected to fold into specific ligand-binding structures (Title).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made that the single-stranded nucleic acid oligomers are selected and amplified to specifically bind any discrete molecule; thus it is irrelevant whether the first reactant is a diene (claim 34) or a dieneophile (claim 35), as Ellington et al teaches that a nucleic.acid could be selected to bind either one.

In addition, the courts have held that the rearrangement of parts within a device is obvious when the arrangement does not specifically modify the operation of the device (*In re Japikse*, 181 F.2d 1019, 86 USPQ 70 (CCPA 1950)). See MPEP §2144.04.

6. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993) in view of Ellington et al (Nature, 1992: 355, pp. 850-852), as evidenced by Mullis et al (U.S. Patent No. 4,965,188, issued 23 October 1990), Paul (U.S. Patent No. 5,236,836, issued 17 August 1993), and Rodwell et al (U.S. Patent No. 5,196,510, issued 23 March 1993) as applied to claim 28 above, and further in view of Woo et al (J. Amer. Chem. Soc., 1991: 113, pp. 5457-5459).

Regarding claim 29, the method of claim 28 is discussed above. Neither Ellington et al nor Hilvert et al teach the use of linker groups.

However, Woo et al teach the use of psoralen probes that are tethered to oligonucleotides (first paragraph, lines 1-3). Woo et al also teach that "the degree to which chemical reactivity can be spatially focused on the target stand and the chemical transformations that can be achieved are of general interest (page 5458, column 1, lines 2-4)."

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method of Hilvert et al in view of Ellington et al with

the linkers of Woo et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method having the added advantage of successfully probing the degree to which chemical reactivity could be focused on the oligonucleotide as explicitly taught by Woo et al (page 5458, column 1, lines 2-4).

7. Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993) in view of Ellington et al (Nature, 1992: 355, pp. 850-852), and Woo et al (J. Amer. Chem. Soc., 1991: 113, pp. 5457-5459) as evidenced by Mullis et al (U.S. Patent No. 4,965,188, issued 23 October 1990), Paul (U.S. Patent No. 5,236,836, issued 17 August 1993), and Rodwell et al (U.S. Patent No. 5,196,510, issued 23 March 1993) as applied to claim 29 above, and in further view of Cload et al (J. Am. Chem. Soc., 1993, 115, pp 5005-5014) as defined by Jolly (Modern Inorganic Chemistry, 1984, McGraw Hill).

Regarding claims 30-31, the method of claim 29 is discussed above. Neither Ellington et al, Hilvert et al, nor Woo teach the use of linker groups having a size in the range of 10 to 1000 Angstroms.

However, Cload et al teach the use of oligonucleotide probes tethered with a neutral polyethylene glycol linker (i.e., claim 31; page 5006, column 1, paragraph 2, lines 4-6). Cload et al also teach that the linker is designed to minimize possible electrostatic effects (page 5006, column 1, paragraph 2, lines 4-6). Finally, the average single bond lengths as described by Jolly (e.g., a C-C bond length of 1.54 Angstroms; Tables 3.5 and 3.6, page 52) clearly establish the length of the linker taught by Cload et al as being between 10 and 1000 Angstroms (i.e., claim 30).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method of Hilvert et al in view of Ellington et al and Woo et al with the polyethylene glycol linkers (i.e., claim 31) having the lengths (i.e., claim 30) of Cload et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method having the added

advantage of minimizing electrostatic effects in the linker as explicitly taught by Cload et al (page 5006, column 1, paragraph 2, lines 4-6).

8. Claims 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993) in view of Ellington et al (Nature, 1992: 355, pp. 850-852), as evidenced by Mullis et al (U.S. Patent No. 4,965,188, issued 23 October 1990), Paul (U.S. Patent No. 5,236,836, issued 17 August 1993), and Rodwell et al (U.S. Patent No. 5,196,510, issued 23 March 1993) as applied to claim 28 above, and further in view of Verdine (PCT International Publication Number WO 93/14108, published 22 July 1993).

Regarding claim 36, the method of claim 28 is discussed above. Neither Ellington nor Hilvert teach the attachment of functional groups.

However, Verdine teaches the attachment of functional groups (e.g., multidentate ligands, page 10, line 32) including substituted thiols and substituted carboxylic acids (page 11) to nucleic acids (page 7, lines 12-13 and Figure 1). Regarding claim 37, the method of claim 36 is described above. Verdine also teaches the attachment of the functional group on a ribose position of said nucleic acid (e.g., at the sugar phosphate backbone; page 17, line 1). Verdine also teaches the attachment of the functional group on a base of said nucleic acid (i.e., claim 38; page 16, lines 31-32), and that the attachment of the functional group on a phosphate position of said nucleic acid at internucleotide phosphorous atoms (i.e., claim 39; page 17, lines 1-2). Verdine also teaches that said functional groups can particularly be used to design and synthesize molecules that specifically bind a desired DNA sequence (page 8, lines 1-5). This allows specific tailoring of the nucleic acid to bind to other molecules.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method of Hilvert et al in view of Ellington et al and Woo et al with the functional groups at the various positions as taught by Verdine with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification

because said modification would have resulted in a method having the added advantage of allowing specific tailoring of a DNA sequence to bind to another molecule as explicitly taught by Verdine (page 8, lines 1-5).

Response to Arguments

Applicant's arguments filed 14 February 2007 (i.e., the "Remarks") have been fully considered but they are not persuasive for the reason(s) listed below.

A. Applicant argues on page 7 of the Remarks that the instantly claimed nucleic acids ligands facilitate the Diels Alder reaction non-catalytically.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., non-catalytic facilitation of a reaction) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Furthermore, a cursory review of the specification yields no limiting definition of what constitutes a "facilitated" reaction, and provides no teaching or example wherein any "facilitated" reaction is specifically prohibited from being facilitated "catalytically."

In addition, the prior art clearly equates the "facilitating" of chemical reactions with catalysis. As noted above, Mullis et al teach defines catalysis as facilitating (column 7, lines 41-45). Paul also equates "catalyze" with "facilitate" (column 1, lines 40-45). Rodwell further defines catalysts as "facilitating" chemical reactions (column 16, lines 10-12). Thus, the catalysts for chemical transformation taught by Ellington et al (page 852, column 2, last paragraph) and the Diels-Alder catalyst as taught by Hilvert et al (column 5, lines 15-17) both encompass the broadly claimed reaction "facilitated by the nucleic acid coupled to said reactant" at the end of claim 1.

B. Applicant also argues on page 8 of the Remarks that the instantly claimed method does not include the nucleic acid being released from the products to bind to new reactants.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., retention of the nucleic acids on the bound products generated by the reaction) are not recited in the rejected claim(s). As noted above, while the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

C. Applicant further argues on page 8 of the Remarks that there is no suggestion to combine the references, or is there a reasonable expectation of success.

The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Hilvert et al teach the Diels Alder reaction is facilitated by a catalytic antibody (Abstract), and that it is beneficial to find a specific catalyst for a Diels-Alder reaction (column 5, lines 15-17), which is a prototype of a broad and important class of pericyclic chemical processes (column 4, lines 45-55). Furthermore, Hilvert et al teach that catalytic antibodies often exhibit severe product inhibition (column 5, lines 5-14); thus, Hilvert et al provide a clear motivation to find catalysts other than antibodies for facilitating the Diels Alder reaction. Hilvert et al do not specifically teach nucleic acid catalysts for facilitating the reaction.

However, Ellington et al teach that nucleic acid aptamers are be new catalysts for chemical transformations that are analogous to catalytic antibodies (page 852, column 2, last paragraph). Ellington et al further teach the nucleic acid aptamers have the added advantage of allowing large numbers (i.e., 2-$3x10^{13}$) of potential catalysts to be produced using common synthetic methodology (i.e., using PCR; page 850, column 1-last paragraph). This increases the probability of finding a superior catalyst.

Thus, the combined teachings of the prior art provide a suggestion to modify the method of Hilvert et al with the teachings of Ellington et al with a reasonable expectation of success. The ordinary

artisan would have been motivated to make such a modification because said modification would have resulted in a method having the added benefit of increasing the probability of finding a superior catalyst by allowing large numbers of potential catalysts to be produced using common synthetic methodology as explicitly taught by Ellington et al page 850, column 1-last paragraph), that simultaneously avoids the severe product inhibition exhibited by antibodies as taught by Hilvert et al (column 4, lines 45-55 and column 5, lines 5-14).

D. Applicant's remaining arguments on pages 9-11 of the Remarks rely on arguments set forth to address the rejections of the claims as obvious over Ellington et al in view of Hilvert et al under 35 U.S.C. 103(a). These arguments are addressed above on pages 5-7. Since the arguments regarding the teachings of Ellington et al and Hilvert et al were not persuasive, the remaining rejections of the dependent claims are maintained.

Conclusion

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

11. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert T. Crow
Examiner
Art Unit 1634

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SUPERVISORY PATENT EXAMINER